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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/008,739	11/09/2001	Tessa A. Castlberry	PC10893AGPR	6055

7590 06/07/2004

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EXAMINER

MURPHY, JOSEPH F

ART UNIT PAPER NUMBER

1646

DATE MAILED: 06/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/008,739

Applicant(s)

CASTLEBERRY ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 13 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 4-13 and 16-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 14 and 15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: Sequence Comparison A.

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## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I, claims 1-3, 14-15, in the reply filed 04/13/2004 is acknowledged. The traversal is on the ground(s) that that it would not be an undue burden on the Examiner to search all of the claims of this application at once because all of the claims are drawn to the same protein, its encoding DNA, or methods of using the same. Applicant alleges that it would not be an undue burden upon the Examiner to search all claims simultaneously. This is not found persuasive because Applicant's attention is directed to MPEP 808.02 which states that "Where the related inventions as claimed are shown to be distinct under the criteria of MPEP 806.05 (c-i), the examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search." As set forth in the Restriction requirement, Group I is classified in class 530, subclass 350; Group II is classified in class 435, subclass 69.1; Group III is classified in class 530, subclass 350, but has a different amino acid sequence than the polypeptide of Group I; Group IV is classified in class 435, subclass 7.2. The separate classification established for each Group demonstrates that each distinct Group has attained recognition in the art as a separate subject for inventive effort, and also a separate field of search. The proteins of Inventions I and III are independent and distinct, each from the other, because they are products which possess characteristic differences in structure and function, and each has an independent use, that is distinct for each invention which cannot be exchanged. In the instant case the proteins have characteristic differences in their structure, as evidenced by the differing amino acid sequences.

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The requirement is still deemed proper and is therefore made FINAL.

***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 14-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a full-length canine androgen receptor of SEQ ID NO: 2, does not reasonably provide enablement for an amino acid sequence of SEQ ID NO: with one or more conservative substitutions therein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to an amino acid sequence of SEQ ID NO: 2 with one or more conservative substitutions therein. Claims 1-2, 14-15 are overly broad since insufficient guidance is provided as to which of the myriad of variant polypeptides will retain the characteristics of caAR. The claims are directed to variant polypeptides. However, Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of caAR. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, As an example of the unpredictable effects of mutations on protein function, Mickle et al. (Mickle JE et al. Genotype-phenotype relationships in cystic fibrosis. Med Clin North Am. 2000 May;84(3):597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause

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CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving rise to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (Voet et al. Biochemistry. 1990. John Wiley & Sons, Inc. pages 126-128 and 228-234) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of only two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000). Since the claims encompass variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. While the claims set forth a functional limitation for the variant polypeptides wherein the polypeptide has canine AR activity,

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this term is indefinite (see *infra*). Additionally, the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for polypeptide variants of caAR, and has not taught how to make polypeptide variants of caAR, it would require undue experimentation of one of skill in the art to make and use the claimed polypeptides.

Claims 14-15 would not be enabled insofar as they read on SEQ ID NO:2. First, the breadth of the claims is excessive since the claims read on all pharmaceutical compositions to treat all diseases. Applicants have provided no guidance or working examples of any methods of treatment for any diseases using this protein, including any data or treatment regimen. Furthermore, it is not predictable to one of ordinary skill in the art how to use a pharmaceutical composition. Applicants can overcome this

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rejection by amending the claims to recite "A composition comprising the proteinaceous molecule according to claim 1 (or 3) and a pharmaceutically acceptable carrier therefor."

Claims 1-2, 14-15 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to an amino acid sequence of SEQ ID NO: 2 with one or more conservative substitutions therein. These are genus claims because the claims are thus directed to variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or

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characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 2 is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.



***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 14-15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in the recitation of the term "canine AR activity". The term "canine AR activity " is not defined by the claim, which gives no definition of what this activity is. The Specification on page 5 sets forth that "activity of caAR" is meant any activity that is measurable by an *in vivo* or *in vitro* caAR assay. However, various biological activities can be attributed to a polypeptide, all of which can be measured by *in vivo* or *in vitro* assays. For example, "canine AR activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. "Canine AR activity" could also be referring to the ability of the fragment to stimulate antibody production. Claims 2-3, 14-15 are rejected insofar as they depend on the recitation of the term "canine AR activity" in claim 1.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Tilley et al. (1989).

Tilley et al. teaches the cloning and expression of the human androgen receptor (page 329, Figure 3). This androgen receptor is 89.6% identical to the caAR of SEQ ID NO: 2 (see Sequence Comparison A, attached). Since claim 1 is drawn to an amino acid with one or more conservative changes, and the human AR of Tilley comprises one or more such changes, claim 1 is anticipated. The Tilley reference also teaches a composition of the human AR in a pharmaceutically acceptable carrier (see page 330, Figure 5), thus claim 14 is anticipated.

### ***Conclusion***

No claim is allowed.

### ***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to be 'J. F. Murphy', written in a cursive style.

Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
May 27, 2004

Application: 10068739

Priority Date: 11-9-2000

Briefed —

Declaration OK

Bib Sheet OK

Title - Novel? OK

Abstract - One Paragraph, no legal jargon OK (n.b. Not "Abstract of the Invention")

IDS — (How Many on Contents? — How many Considered? —)

RSL OK

Election Complete? OK

Search Notes? OK EAST OK STN OK

Index of Claims OK

101 - Utility? Hand of Man? - Even in Methods

Isolated? Recombinant?

112 first and second

Patent Profanity:

Pharmaceutical Composition - 1st scope  
Naturally occurring - 1st  
Allelic Variant - 1st scope and written desc  
Host cell - not isolated - 1st Eck and Wilson  
Fragment - No function - 1st Written Desc and Scope  
Methods: Do the steps=the Preamble 112 2  
X Contigs - No function - 1st Written Desc and Scope  
% Identity = No Function - 1st Written Desc and Scope  
Stringent - 2nd  
Essentially - 2nd  
Acronyms - Objection or 2nd  
Modulates - 2nd

Lack of Antecedent Basis  
Failure to Further Limit - Objection  
Prevent  
Treat

102 - Easy 102, do the claims read on:

Random Primers  
Single Amino Acids  
  
Inherency of Methods  
Product by Process, Examine the Product  
Inherent Properties

103

First Reference Teaches...  
First Reference Does Not teach...  
  
Second Reference Teaches  
Therefore, it would be obvious...  
Motivation and Expectation  
Of success

M, ZKDC ✓  
VOLT ✓  
YAK ✓

## Sequence Comparison A

### RESULT 1

A39248  
 androgen receptor - human  
 C;Species: Homo sapiens (man)  
 C;Date: 04-Oct-1991 #sequence\_revision 04-Oct-1991 #text\_change 24-Nov-1999  
 C;Accession: A39248; A30328; A40109; A60946; A34942; A27653; A40108; A40494; A32224;  
 A40715; A37124  
 A;Accession: A40494  
 A;Molecule type: mRNA  
 A;Residues: 1-74,79-89,'H',90-472,'GGG',473-474,'E',476-644,'N',646-919 <CH2>  
 A;Cross-references: GB:M23263  
 R;Tilley, W.D.; Marcelli, M.; Wilson, J.D.; McPhaul, M.J.  
 Proc. Natl. Acad. Sci. U.S.A. 86, 327-331, 1989  
 A;Title: Characterization and expression of a cDNA encoding the human androgen receptor.  
 A;Reference number: A32224; MUID:89098909; PMID:2911578  
 A;Accession: A32224  
 A;Molecule type: mRNA  
 A;Residues: 1-77,79-211,'R',213-471,473-919 <TIL>  
 A;Cross-references: GB:M21748; GB:J04150; NID:g178871; PIDN:AAA51771.1; PID:g178872  
 R;Mowszowicz, I.; Lee, H.J.; Chen, H.T.; Mestayer, C.; Portois, M.C.; Cabrol, S.;  
 Mauvais-Jarvis, P.; Chang, C.  
 Mol. Endocrinol. 7, 861-869, 1993  
 A;Title: A point mutation in the second zinc finger of the DNA-binding domain of the  
 androgen receptor gene causes complete androgen insensitivity in two siblings with  
 receptor-positive androgen resistance.  
 A;Reference number: A40715; MUID:94019395; PMID:8413310  
 A;Accession: A40715  
 A;Status: not compared with conceptual translation  
 A;Molecule type: DNA  
 A;Residues: 557-614,'H',616-624 <MOW>  
 A;Cross-references: PIDN:AAB28340.1; PID:g425580  
 C;Genetics:  
 A;Gene: GDB:AR  
 A;Cross-references: GDB:120556; OMIM:313700  
 A;Map position: Xq11-Xq12  
 A;Introns: 538/2; 589/1; 628/1; 724/1; 772/2; 816/1; 868/3  
 C;Superfamily: unassigned erba-related proteins; erba transforming protein homology  
 C;Keywords: DNA binding; steroid binding; transcription regulation; zinc finger  
 F;557-815/Domain: erba transforming protein homology <ERBA>  
 F;559-579/Region: zinc finger  
 F;595-619/Region: zinc finger

Query Match 89.6%; Score 4321; DB 2; Length 919;  
 Best Local Similarity 87.6%; Pred. No. 5.2e-230;  
 Matches 822; Conservative 20; Mismatches 46; Indels 50; Gaps 5;

Qy	1	MEVQLGLGRVYPRPPSKTYRGAFQNLFSQSVREVIQNPGRHPEAVSAAPGAHL-----	54
Db	1	MEVQLGLGRVYPRPPSKTYRGAFQNLFSQSVREVIQNPGRHPEASAAPPGASLLLLLQQQ	60
Qy	55	-----QQQQQQQQQETSPPRQQQQQQQDDGSPQAQSRGPTGYLALDEEQQPSQQRS	106
Db	61	QQQQQQQQQQQQQQQQQETSPPR-QQQQQQGEDGSPQAHRRGPTGYLVLDEEQQPSQPQS	119
Qy	107	ASKGHPESACVPEPGVTSATGKGLQQQPAPPDENDSAAPSTLSLLGPTFPGLSSCSTDL	166
Db	120	ALBCHPERGCVPEPGAAVAASKGLPQQLPAPPDEDDSAAPSTLSLLGPTFPGLSSCSADL	179
Qy	167	KDILSEAGTMQLLQQRQQQQQQQQQQQQQQQQQEVVSESSSGRAREAAAGASTSSKD	226
Db	180	KDILSEASTMQLL-----QQQQQEAQVSESSSGRAREASGAPTSSKD	221
Qy	227	SYLGGSSTISDSAKELCKAVSVSMGLGVEALEHLSPEQLRGDCMYAPLLGGPPAVR--P	284
Db	222	NYLGGTSTISDNAELCKAVSVSMGLGVEALEHLSPEQLRGDCMYAPLLGVPPAVRPTP	281
Qy	285	CAPLAECKGSLDDGPGKGTEETAFFSPFKAGYAKGLDGDLSGSSSSEAGSGTLEMP	344

Db 282 CAPLAECKGSLDDDSAGKSTEDTAEYSPFKGGYTKGLEGESLGCSGSAAAGSSGTLELPS 341  
 Qy 345 TSLYKSGALDEAAAYQSRDYNNFPLSLGGPPPPPPHPPHTRIKLENPLDYGSAAAA 404  
 |||||:|||||  
 Db 342 TSLYKSGALDEAAAYQSRDYNNFPLALAGPPPPPPHPPHTRIKLENPLDYGSAAAA 401  
 Qy 405 AQCRYGDLASLHGAGAAGPSSGSPSATSSSWHTLFTAEEGQLYGCGGSGGSAGD-- 462  
 |||||:|||||  
 Db 402 AQCRYGDLASLHGAGAAGPSSGSPSAAASSWHTLFTAEEGQLYGCGGSGGSGGGGGG 461  
 Qy 463 -----GSVAPYGYTRPPQGLAQEGDFPPPDVWYPGGVVSrvPFPSPSCVKS 509  
 |:|||||:|||||  
 Db 462 GGGGGGGGGGEGAGAVAPYGYTRPPQGLAQESDFTAPDVWYPGGMVSRVPYPSPTCVKS 521  
 Qy 510 EMGSWMESYSGPYGDMRLETARDHVLPIDYFFPPQKTCCLICGDEASGCHYGALTCGSKV 569  
 ||| |:|||||  
 Db 522 EMGPWMSYSGPYGDMRLETARDHVLPIDYFFPPQKTCCLICGDEASGCHYGALTCGSKV 581  
 Qy 570 FFKRAAEGKQKYLCA SRNDCTIDKFRRNKNCPSCLRLKCYEAGMTLGARKLKKLGNLKLQE 629  
 |||||:|||||  
 Db 582 FFKRAAEGKQKYLCA SRNDCTIDKFRRNKNCPSCLRLKCYEAGMTLGARKLKKLGNLKLQE 641  
 Qy 630 EGEASNVTSPTEETQKLTVSHIEGYECQPIFLNVLEAIEPGVVCAGHDNNQPSFAALL 689  
 |||||:|||||  
 Db 642 EGEASSTSPTEETTQKLTVSHIEGYECQPIFLNVLEAIEPGVVCAGHDNNQPSFAALL 701  
 Qy 690 SSLNELGERQLVHVVKWAKALPGFRNLHVDDQMAVIQYSWMGLMVFAMGWSFTNVNSRM 749  
 |||||:|||||  
 Db 702 SSLNELGERQLVHVVKWAKALPGFRNLHVDDQMAVIQYSWMGLMVFAMGWSFTNVNSRM 761  
 Qy 750 LYFAPDLVFNEYRMHKS RMYSQCVRMRHLSQEFGLQITPQEFCLMKALLFSIIPVDGL 809  
 |||||:|||||  
 Db 762 LYFAPDLVFNEYRMHKS RMYSQCVRMRHLSQEFGLQITPQEFCLMKALLFSIIPVDGL 821  
 Qy 810 KNQKFFDEL RMNYIKELDR IIACKRKNPTSCSRRFYQLTKLLDSVQPIARELHQFTFDLL 869  
 |||||:|||||  
 Db 822 KNQKFFDEL RMNYIKELDR IIACKRKNPTSCSRRFYQLTKLLDSVQPIARELHQFTFDLL 881  
 Qy 870 IKSHMVSVD FPEMMAEII SVQVPKILSGKV KPIYFHTQ 907  
 |||||:|||||  
 Db 882 IKSHMVSVD FPEMMAEII SVQVPKILSGKV KPIYFHTQ 919